



K1532

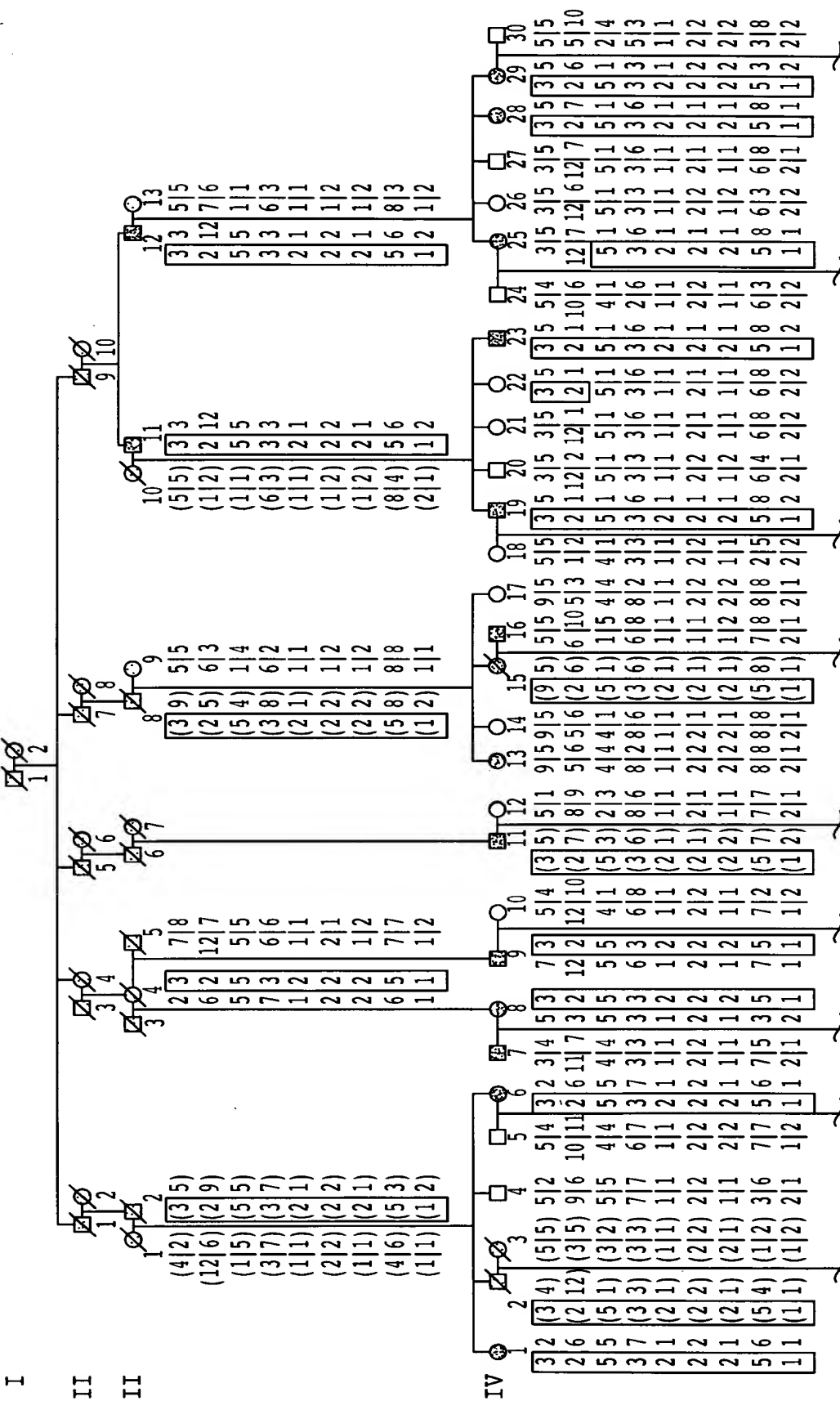


FIG. 1A



KVLQT1 - A Long QT Syndrome Gene
Mark T. KEATING et al. - Atty Ref. 2323-151
SN 09/597,732, filed 19 June 2000

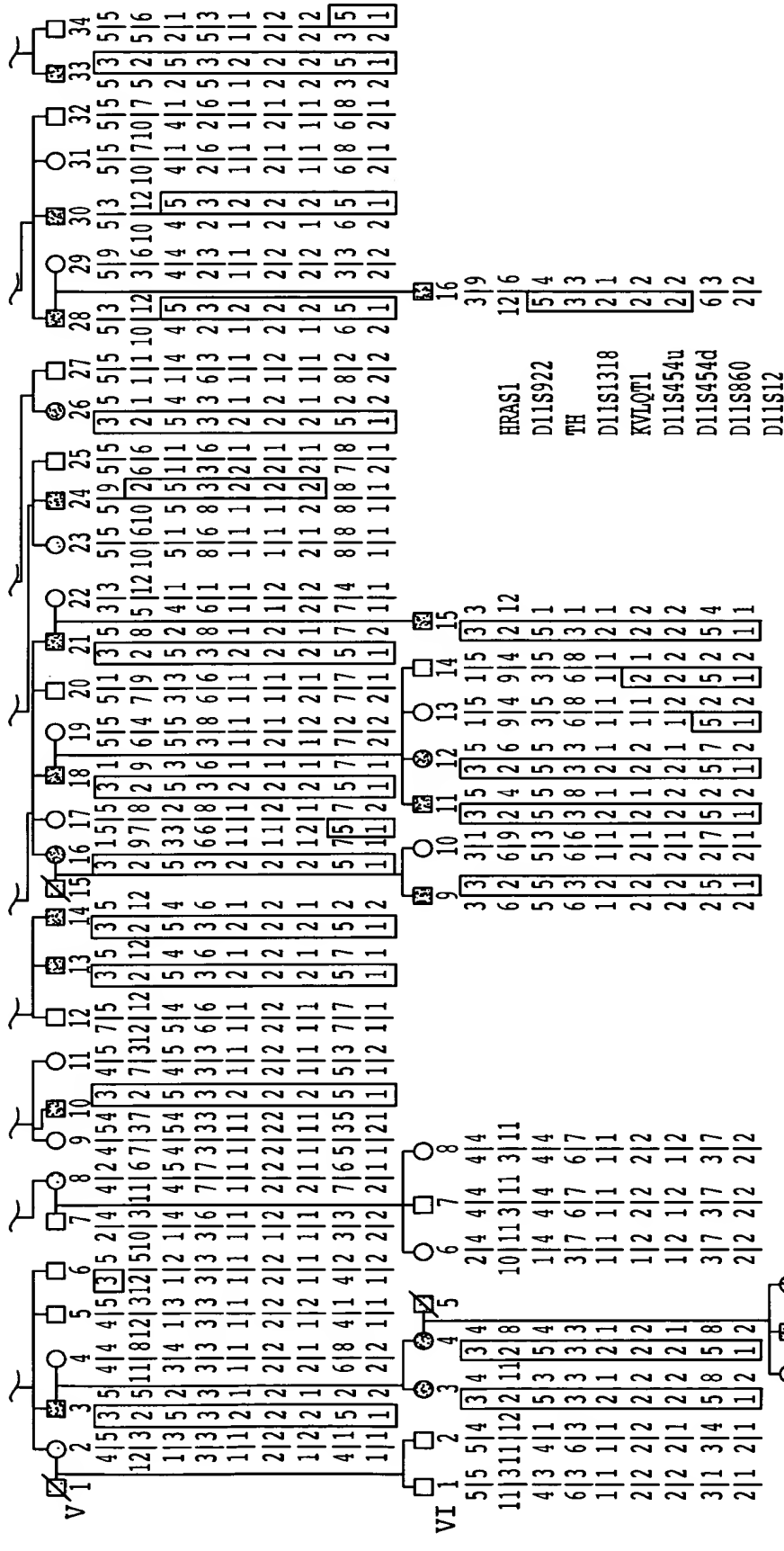


FIG. 1B

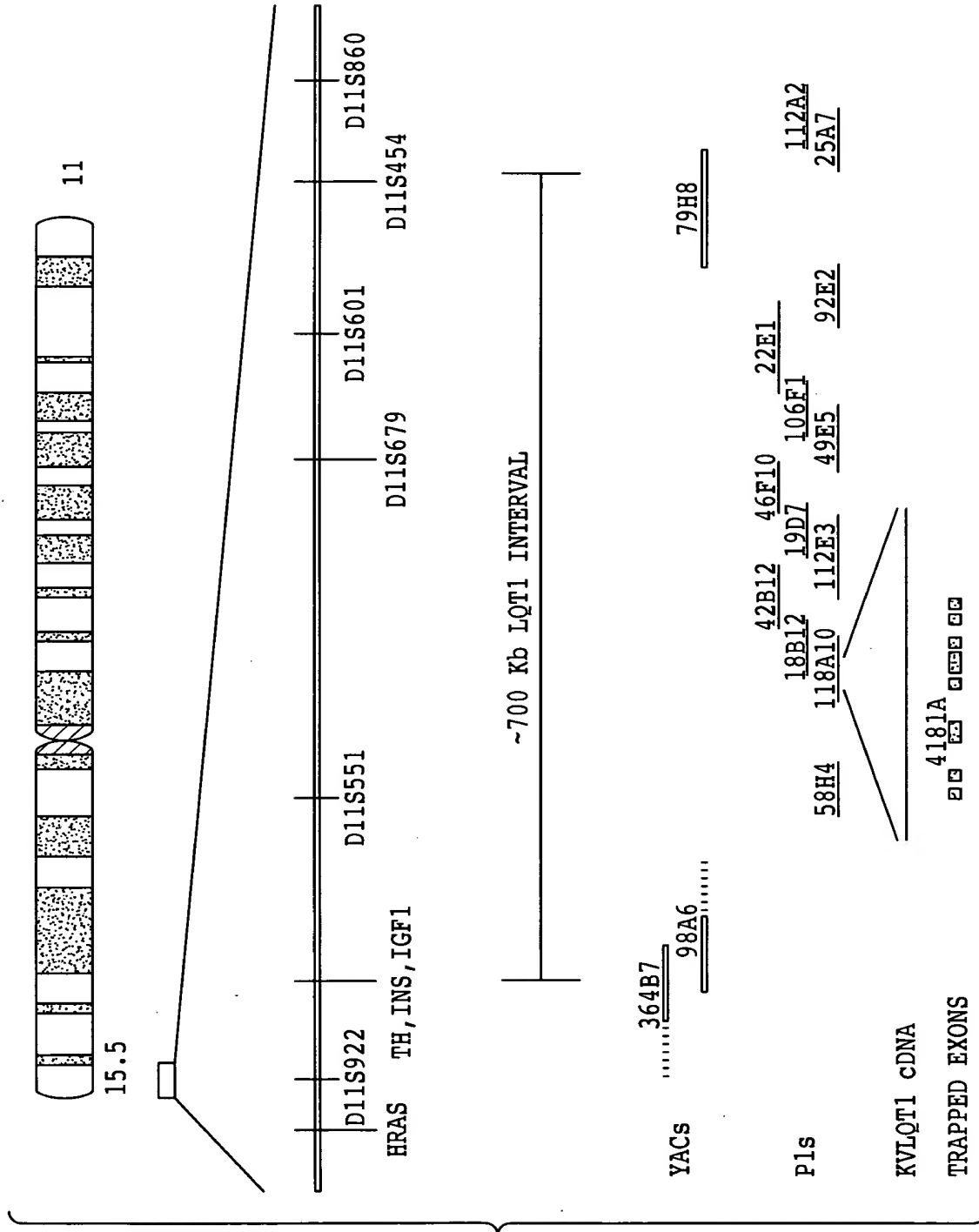


FIG. 2

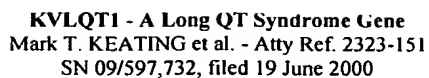


FIG. 3



KVLQT1 - A Long QT Syndrome Gene
Mark T. KEATING et al. - Atty Ref. 2323-151
SN 09/597,732, filed 19 June 2000

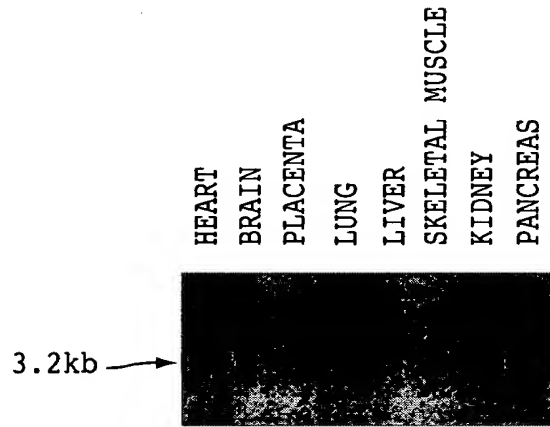


FIG. 4



CTGCCCCCTCCGGCCCCGCCCCGAGCGCCCGGGCTGGGCGCGGAGCGCCCCCGCGGGGGCTGGCAGCAGTGGCTGCC-81
CGCACTGCGCCCGGGCGCTCGCCTTCGCTGCAGCTCCCGGTGCGCGCGCTCGGGCGGGCCCCCGGCAGGCCCTCCTCGTT-162
ATGGCCGCGGCCCTCCTCCCCGCGCAGGGCCGAGAGGAAGCGCTGGGGTTGGGGCCGCTGCCAGCGCCCCGGCGGGGCAGC-243
M A A A S S P P R A E R K R W G W G R L P G A R R G S -27
GCGGGCTGGCCAAGAAGTCCCCCTTCTCGCTGGAGCTGGCGGAGGGCGGGCGGGCGGGCGGCTCTACGCGCCATC-324
A G L A K K C P F S L E L A E G G P A G G A L Y A P I -54
GCGCCCGGCGCCCCAGGTCCCGCGCCCCCTGCGTCCCGCGCGCGCGCGCGCCCCAGTTGCCTCCGACCTTGGCCCG-405
A P G A P G P A P P A S P A A P A A P P V A S D L G P -81
CGGCCGCGGTGAGCTAGACCCGCGCGTCTCCATCTACAGCACGCGCGCGCGCGTGTGGCGCGCACCCACGTCCAGGGC-486
R P P V S L D P R V S I Y S T R R P V L A R T H V Q G -108
CGCGTCTACAACCTCCTCGAGCGTCCACCGGCTGGAATGCTTCGTTTACCACCTTCGCGCTCTCCTCATCGTCTGGTC-567
R V Y N F L E R P T G W K C F V Y H F A V F L I V L V -135
TGCCTCATCTTCAGCGTGCTGTCCACCATCGAGCAGTATGCCGCCCTGGCCACGGGGACTCTCTTCTGGATGGAGATCGTG-648
C L I F S V L S T I E Q Y A A L A T G T L F W M E I V -162
CTGGTGGTGTCTTCGCGGACGGAGTACGTGGTCCGCCTCTGGTCCCGCGGCTGCCGCGAGCAAGTACGTGGGCTCTGGGGG-729
L V V F F G T E Y V V R L W S A G C R S K Y V G L W G -189
CGGCTGCGCTTTGCCCGGAAGCCCATTTCCATCATCGACCTCATCGTGGTTCGTGGCTCCATGGTGGTCTCTGCGTGGGC-810
R L R F A R K P I S I I D L I V V V A S M V V L C V G -216
TCCAAGGGGAGGTGTTTGGCCATCGGCCATCAGGGGCATCCGCTTCTGCGATCCTGAGGATGCTACACGTCGACCGC-891
S K G Q V F A T S A I R G I R F L Q I L R M L H V D R -243
CAGGGAGGCACCTGGAGGCTCCTGGGCTCCGTGGTCTTCATCCACCGCCAGGAGCTGATAACCACCTGTACATCGGCTTC-972
Q G G T W R L L G S V V F I H R Q E L I T T L Y I G F -270
CTGGGCTCATCTTCTCCTCGTACTTTGTGTACTGGCTGAGAAGGACCGGTGAACGAGTCAGGCCGCGTGGAGTTCGGC-1053
L G L I F S S Y F V Y L A E K D A V N E S G R V E F G -297
AGCTACGCAGATGCGCTGTGGTGGGGGGTGGTACAGTCAACCACCATCGGCTATGGGGACAAGGTGCCCCAGACGTGGGTC-1134
S Y A D A L W W G V V T V T T I G Y G D K V P Q T W V -324
GGGAAGACCATCGCCTCCTGCTTCTGTCTTTGCCATCTCCTTCTTTGCGCTCCAGCGGGGATTCTTGGCTCGGGGTTT-1215
G K T I A S C F S V F A I S F F A L P A G I L G S G F -351
GCCCTGAAGGTGCAGCAGAAGCAGAGGCAGAAGCACTTCAACCGGCAGATCCCGCGGCAGCCTCACTCATTACAGCCGCA-1296
A L K V Q Q K Q R Q K H F N R Q I P A A A S L I Q T A -378
TGGAGGTGCTATGCTGCCGAGAACCCCGACTCCTCCACCTGGAAGATCTACATCCGGAAGGCCCGGAGCCACACTCTG-1377
W R C Y A A E N P D S S T W K I Y I R K A P R S H T L -405
CTGTACCCAGCCCCAAACCAAGAAGTCTGTGGTGGTAAAGAAAAAAGTTCAAGCTGGACAAAGACAATGGGGTGA-1458
L S P S P K P K K S V V V K K K K F K L D K D N G V T -432
CCTGGAGAGAAGATGCTCACAGTCCCCATATCACGTGCGACCCCCAGAAGAGCGGCGGCTGGACCACTTCTCTGTGAC-1539
P G E K M L T V P H I T C D P P E E R R L D H F S V D -459
GGCTATGACAGTTCTGTAAGGAAGAGCCCAACACTGCTGGAAGTGAGCATGCCCCATTTTCATGAGAACCAACAGCTTCGCC-1620
G Y D S S V R K S P T L L E V S M P H F M R T N S F A -486
GAGGACCTGGACCTGGAAGGGGAGACTCTGTGACACCCATCACCCACATCTCACAGCTGCGGGAACACCATCGGGCCACC-1701
E D L D L E G E T L L T P I T H I S Q L R E H H R A T -513
ATTAAGGTCAATTCGACGCATGCAGTACTTTGTGGCCAAGAAGAAATTCAGCAAGCGCGGAAGCCTTACGATGTGCGGGAC-1782
I K V I R R M Q Y F V A K K K F Q Q A R K P Y D V R D -540
GTCATTGAGCAGTACTCGCAGGGCCACCTCAACCTCATGGTGGCATCAAGGAGCTGCAGAGGAGGCTGGACCACTCCATT-1863
V I E Q Y S Q G H L N L M V R I K E L Q R R L D Q S I -567

FIG. 5A



GGGAAGCCCTCACTGTTTCATCTCCGTCTCAGAAAAGAGCAAGGATCGCGGCAGCAACACGATCGGCGCCCGCCTGAACCGA-1944
G K P S L F I S V S E K S K D R G S N T I G A R L N R -594

GTAGAAGACAAGGTGACGCAGCTGGACCAGAGGCTGGCACTCATCACCAGATGCTTCACCAGCTGCTCTCCTTGACGGT-2025
V E D K V T Q L D Q R L A L I T D M L H Q L L S L H G -621
GGCAGCACCCCGGCAGCGGGCGGCCCCCAGAGAGGGCGGGGCCACATCACCAGCCCTGCGGCAGTGGCGGCTCCGTC-2106
G S T P G S G G P P R E G G A H I T Q P C G S G G S V -648
GACCCTGAGCTCTTCTGCCAGCAACACCTGCCACCTACGAGCAGCTGACCGTGCCAGGAGGGGCCCCGATGAGGGG-2187
D P E L F L P S N T L P T Y E Q L T V P R R G P D E G -675
TCCTGAGGAGGGGATGGGGCTGGGGGATGGGCCTGAGTGAGAGGGGAGGCCAAGAGTGGCCCCACCTGGCCCTCTCTGAAG-2268
S * -676
GAGGCCACCTCCTAAAAGGCCAGAGAGAAGAGCCCCACTCTCAGAGGCCCCAATACCCCATGGACCATGCTGTCTGGCAC-2349
AGCCTGCACTTGGGGGCTCAGCAAGGCCACCTCTTCTGGCCGGTGTGGGGGCCCCGTCTCAGGTCTGAGTTGTTACCCCA-2430
AGCGCCCTGGCCCCACATGGTGATGTTGACATCACTGGCATGGTGGTTGGGACCCAGTGGCAGGGCACAGGGCCTGGCCCC-2511
ATGTATGGCCAGGAAGTAGCACAGGCTGAGTGACAGGCCACCTGCTTGGCCCAGGGGGCTTCCTGAGGGGAGACAGAGCA-2592
ACCCCTGGACCCAGCCTCAAATCCAGGACCTGCCAGGCACAGGCAGGGCAGGACCAGCCACGCTGACTACAGGGCCAC-2673
CGGCAATAAAAGCCCAGGAGCCCATTTGGAGGGCCTGGGCCTGGCTCCCTCACTCTCAGGAAATGCTGACCCATGGGCAGG-2754
AGACTGTGGAGACTGCTCCTGAGCCCCAGCTTCCAGCAGGAGGGACAGTCTCACCATTCCCCAGGGCACGTGGTTGAGT-2835
GGGGGAACGCCCCTTCCCTGGGTTAGACTGCCAGCTCTTCTAGCTGGAGAGGAGCCCTGCCTCTCCGCCCCCTGAGCCC-2916
ACTGTGCGTGGGGCTCCCGCCTCCAACCCCTCGCCAGTCCCAGCAGCCAGCCAAACACAGAAAGGGGACTGCCACCTCC-2997
CCTTGCCAGCTGCTGAGCCGAGAGAAGTGACGGTTCCTACACAGGACAGGGGTTCCTTCTGGGCATTACATCGCATAGAA-3078
ATCAATAATTTGTGGTGATTTGGATCTGTGTTTAAATGAGTTTCACAGTGTGATTTTGATTATTAATTGTGCAAGCTTTTC-3159
CTAATAAACGTGGAGAATCAC(A)n -3180

FIG. 5B

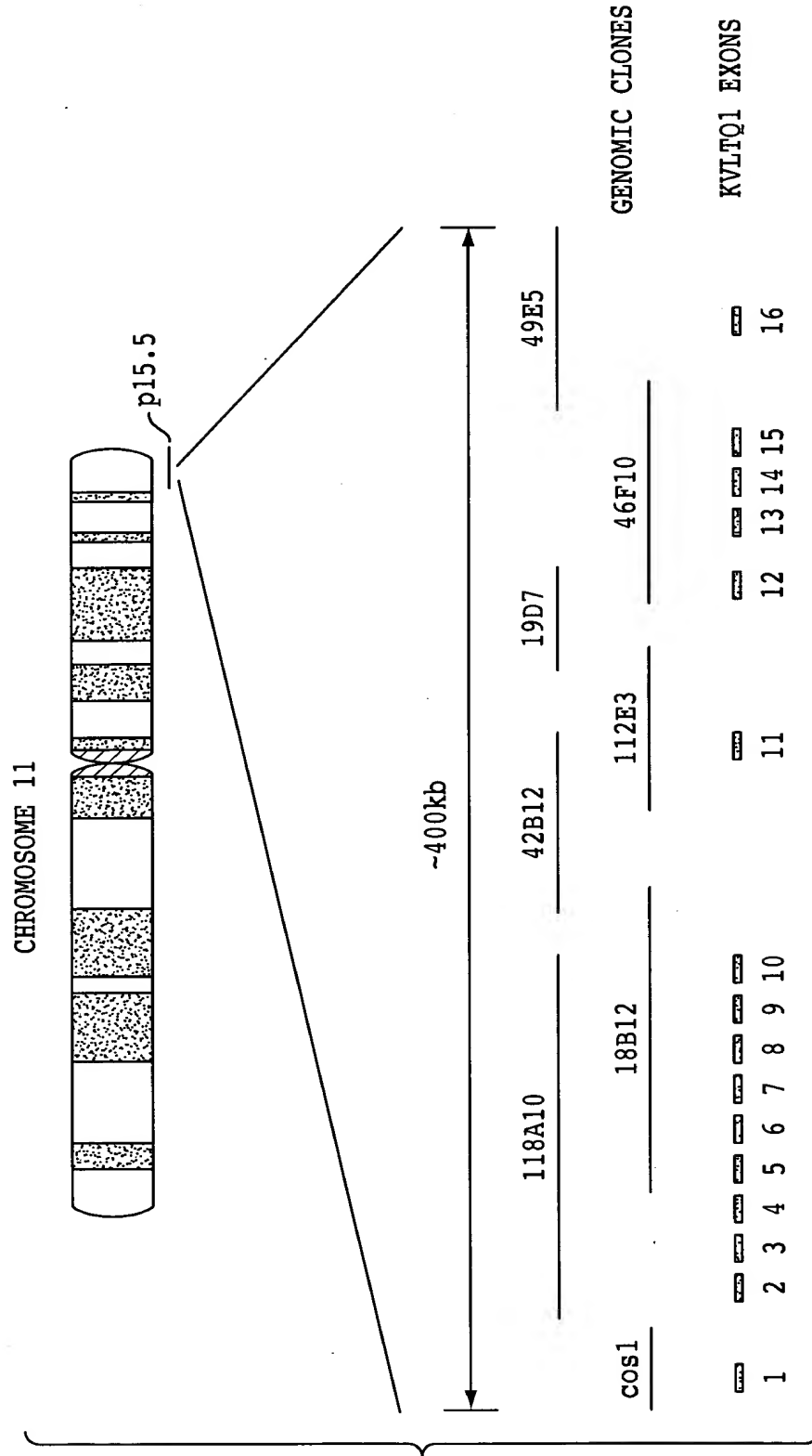


FIG. 6

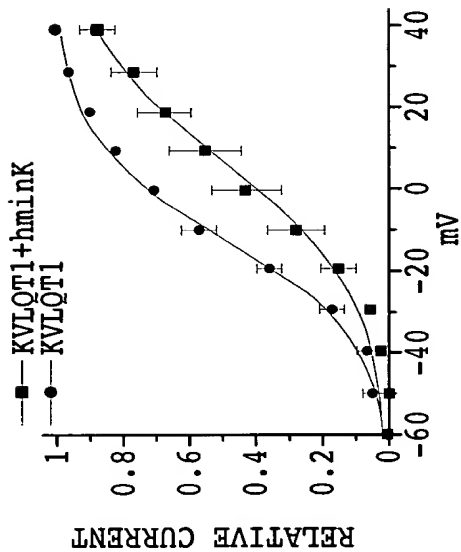


FIG. 7B

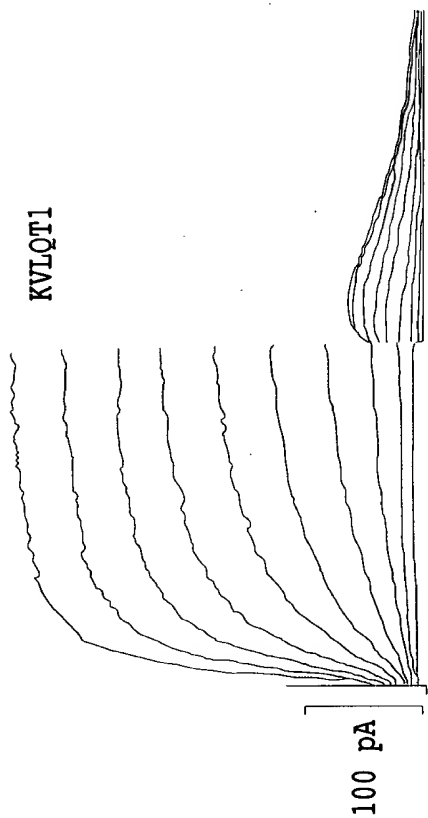


FIG. 7A

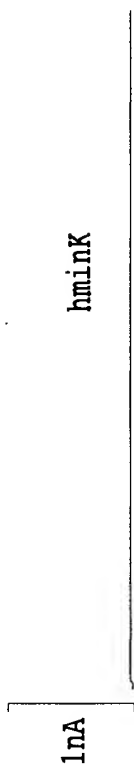


FIG. 7C

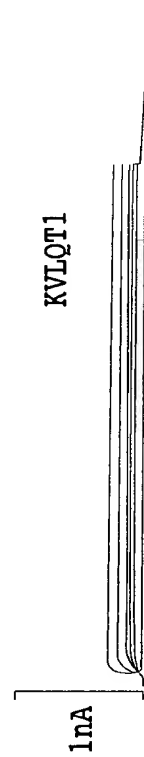


FIG. 7D

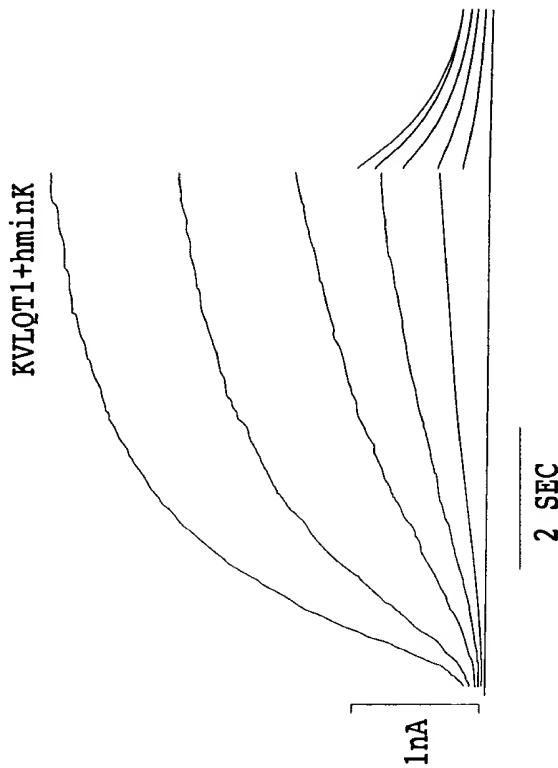
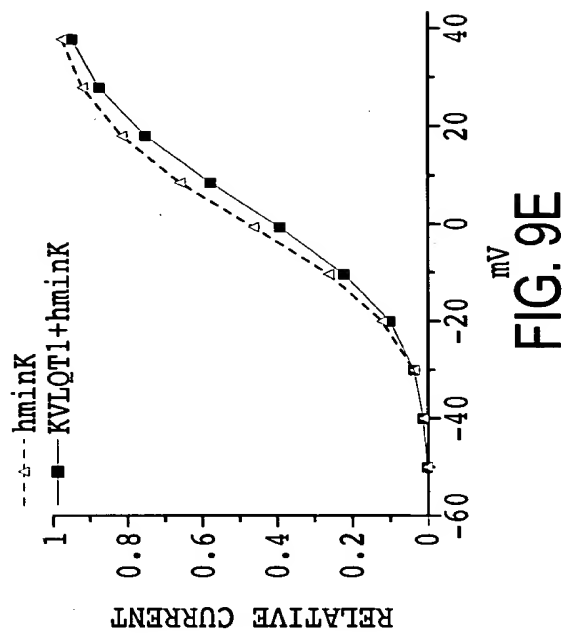
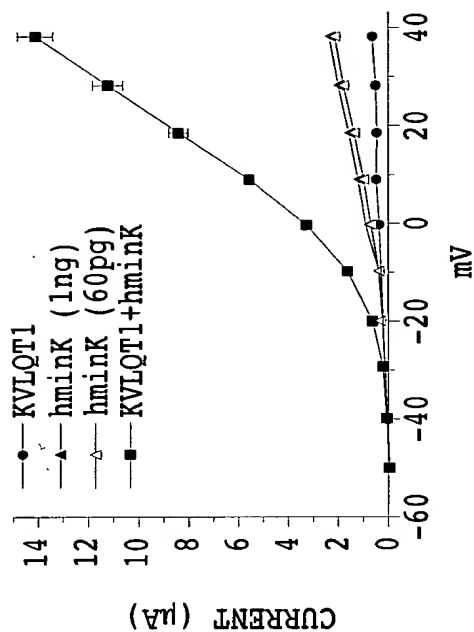
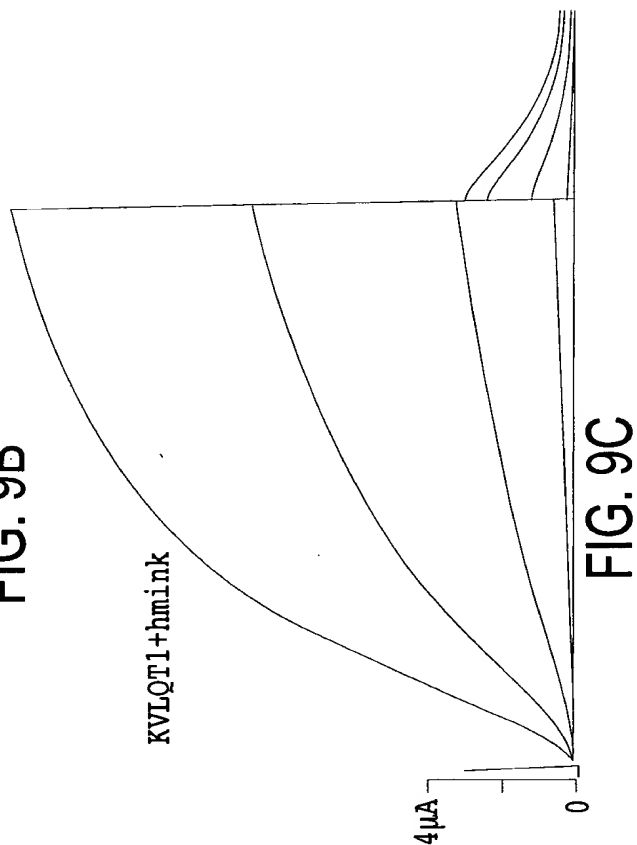
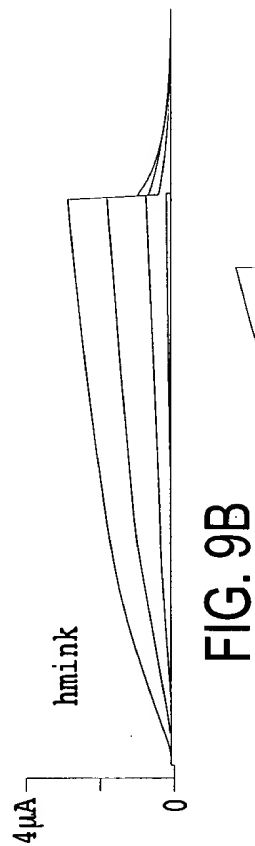
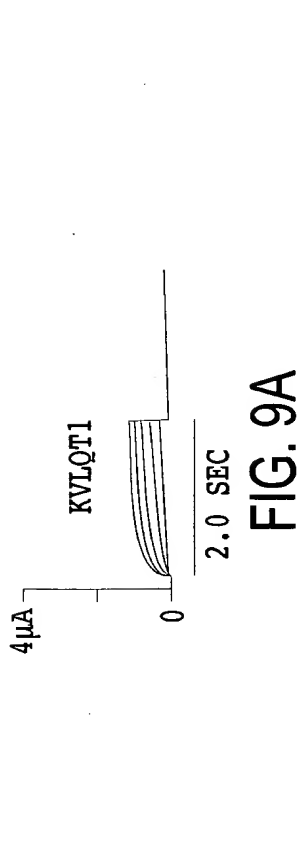


FIG. 7E



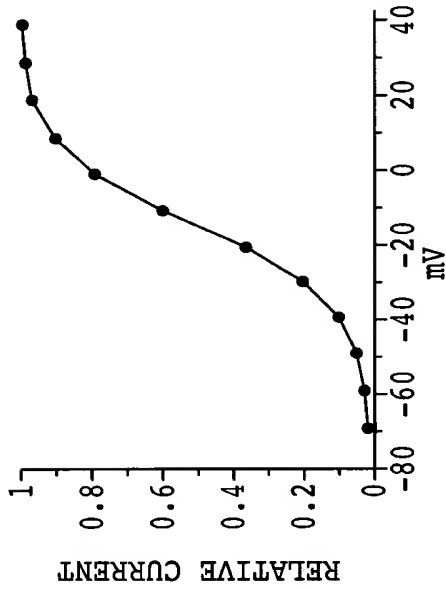


FIG. 8B

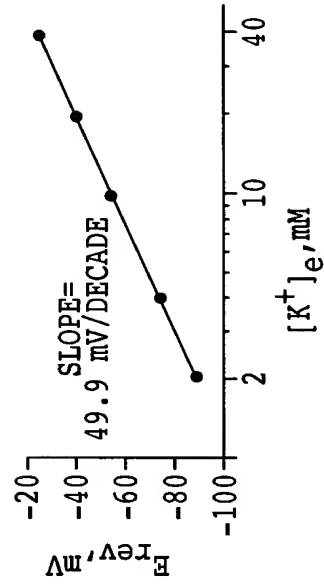


FIG. 8C

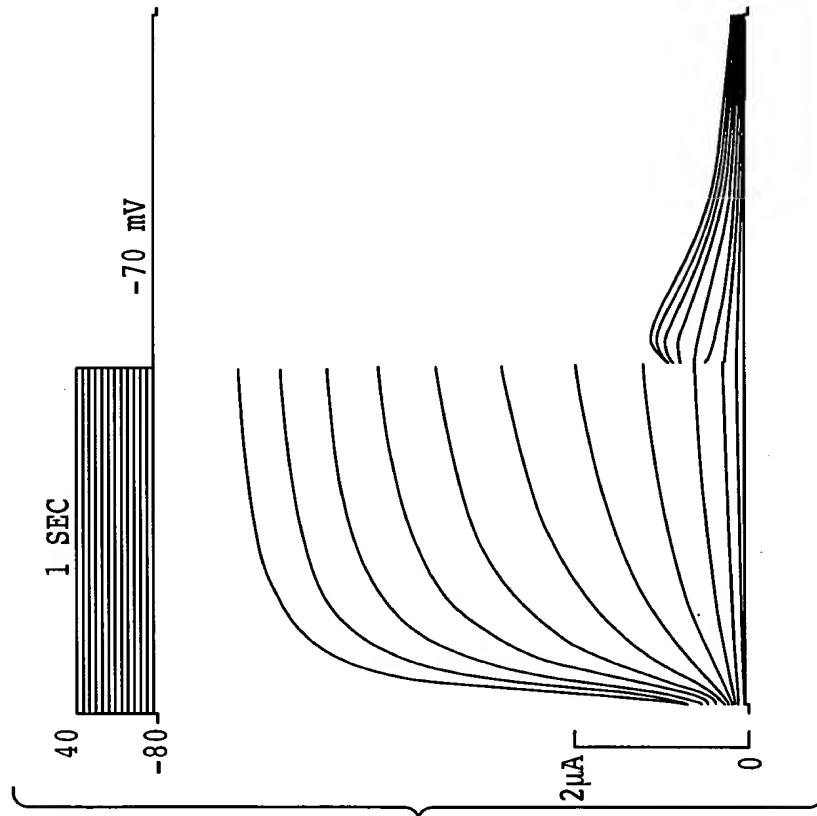


FIG. 8A



KVLQT1 - A Long QT Syndrome Gene
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XENOPUS MNENAINSLYEAIPLPDGSSNGRQEDRQANSFELKRETLVATDPPRPT

HUMAN QGRVYNFLERPTGWKCFVYHFAVFLIVL
|||||

XENOPUS INLDPRVSIYSGRRPLFSRTNIQGRVYNFLERPTGWKCFVYHFTVFLIVL

HUMAN S1_____S2_____
VCLIFSVLSTIEQYAALATGTLFWMEIVLVVFFGTEYVVRLWSAGCRSKY
|||||

XENOPUS ICLIFSVLSTIQYNNLATETLFWMEIVLVVFFGAEYVVRLWSAGCRSKY

HUMAN VGLWGRLRFARKPISIIDLIVVVASMVVLCVGSKGQVFATSAIRGIRFLQ
|||||

XENOPUS VGVWGRLRFARKPISVIDLIVVVASVIVLCVGSNGQVFATSAIRGIRFLQ
A

HUMAN ILRMLHVDRQGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE
|||||

XENOPUS ILRMLHVDRQGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE

HUMAN Pore_____
KDAVNESGRVEFGSYADALWWGVVTVTTIGYGDKVPQTWVGKTIASCFSV
|||

XENOPUS KDAIDSSGEYQFGSYADALWWGVVTVTTIGYGDKVPQTWIGKTIASCFSV

HUMAN S6_____
FAISFFALPAGILGSGFALKVQOKQKQKHFNRQIPAAASLIQTAWRCYAA
|||||

XENOPUS FAISFFALPAGILGSGFALKVQOKQKQKHFNRQIPAAASLIQTAWRCYAA

HUMAN ENPDSSTWKIYIRKAPRSHTLLSPSPKPKKS VVVKKKKFKLDKDNVTPG
|||||

XENOPUS ENPDSATWKIYIRKQSRNHHIMSPSP

HUMAN EKMLTVPHITCDPPEERRLDHFSVDGYDSSVRKSPTLLEVSMPHFMRTNS

HUMAN FAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKKKFQOARK

HUMAN PYDVRDVIEQYSQGHNLNMRVIKELQRRLDQSIGKPSLFISVSEKSKDRG

HUMAN SNTIGARLNRVEDKVTQLDQRLALITDMLHQLLSLHGGSTPGSGGPPREG

HUMAN GAHITQPCGSGGSVDPELFLPSNTLPTYEQLTVPRRGPDDEGS

FIG. 10

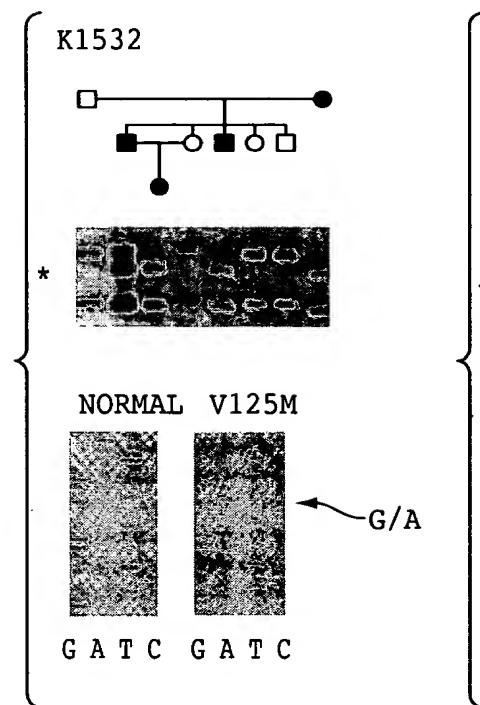


FIG. 11A

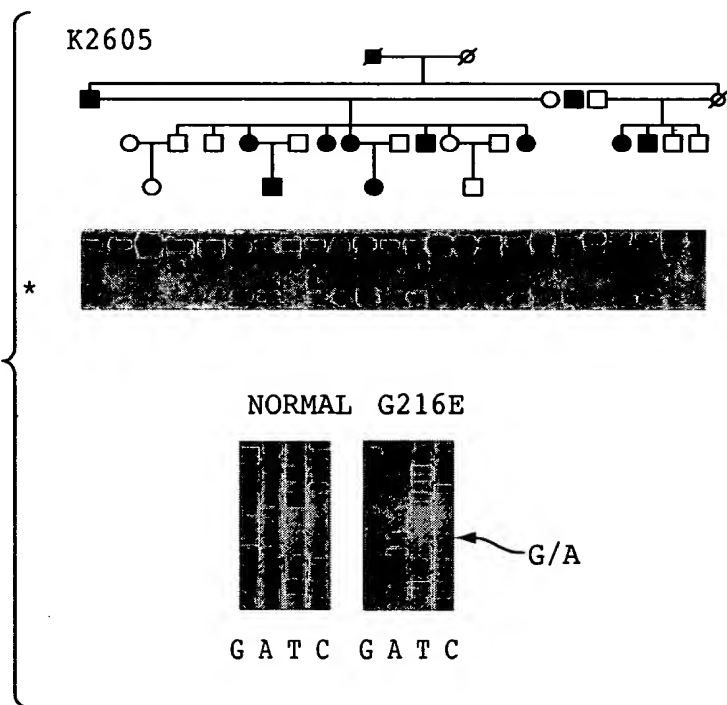


FIG. 11B

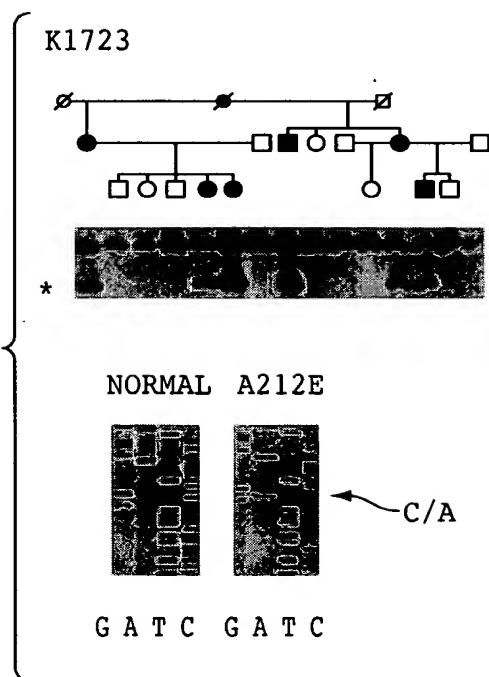


FIG. 11C

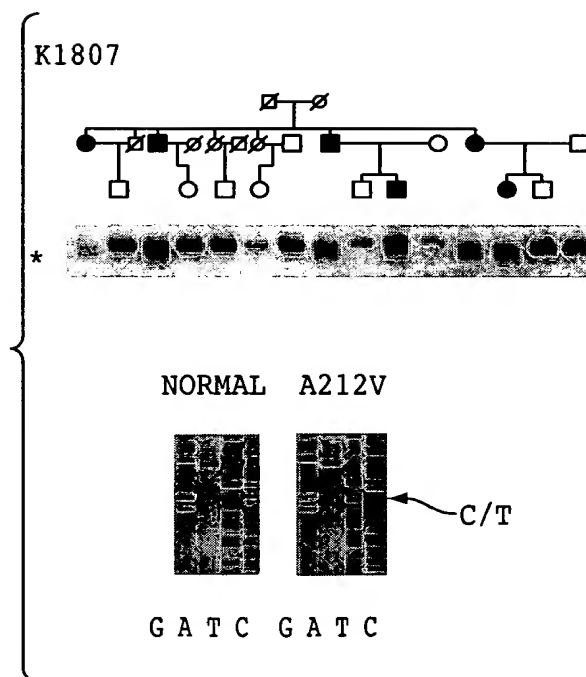
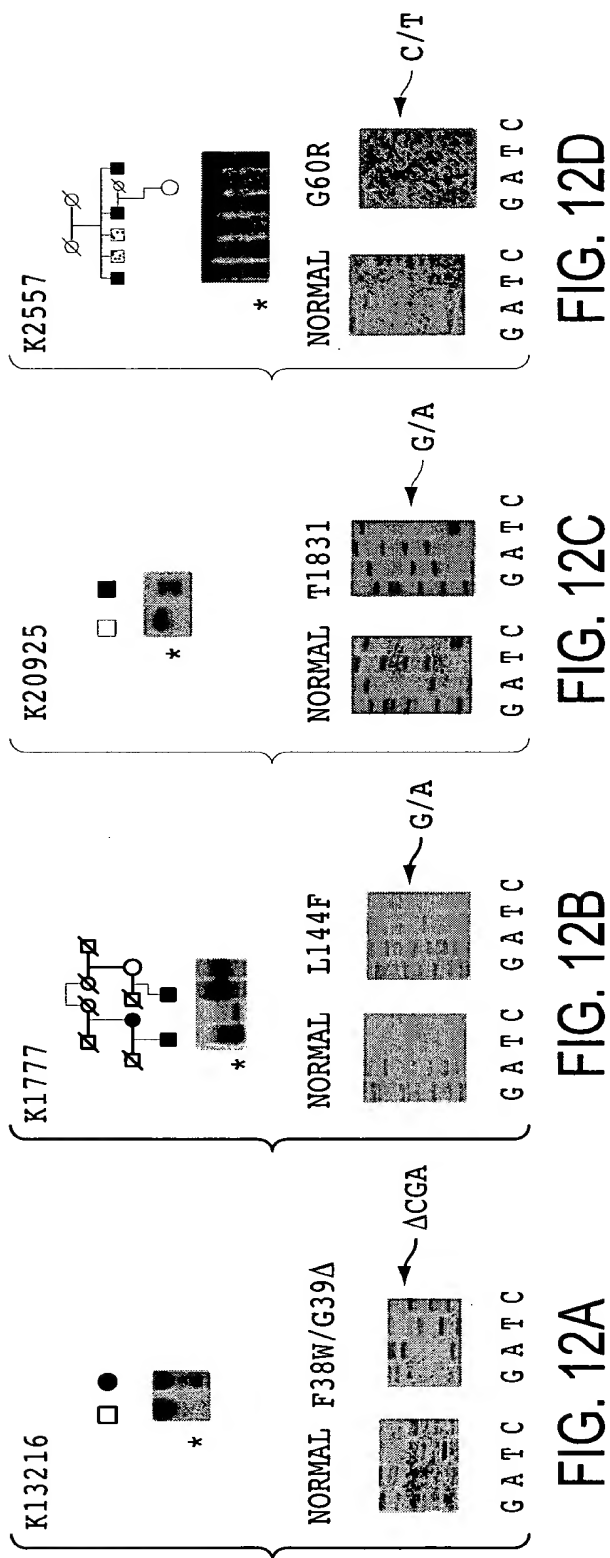


FIG. 11D



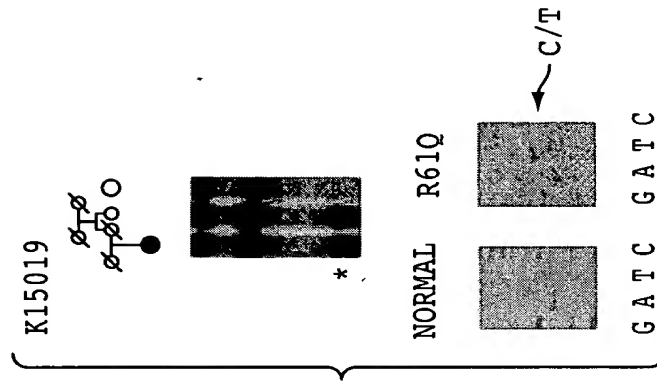


FIG. 12G

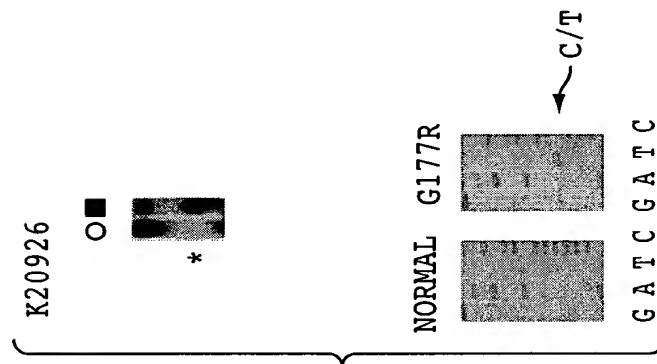


FIG. 12F

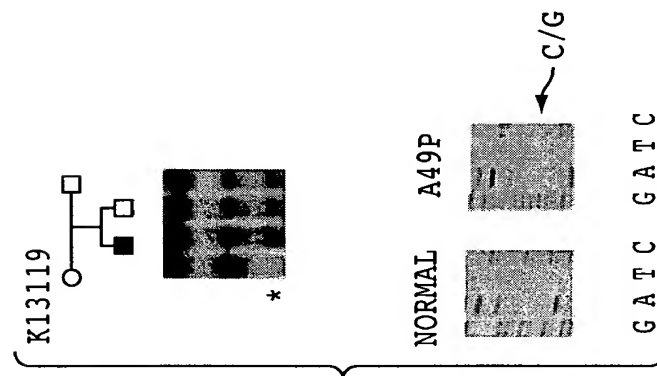


FIG. 12E

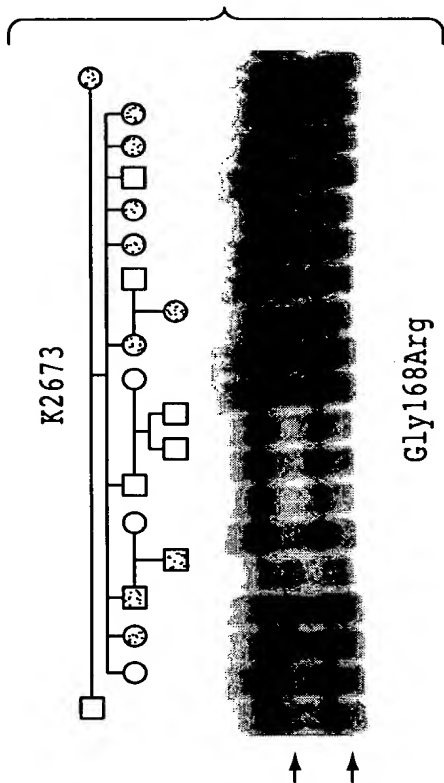


FIG. 12I

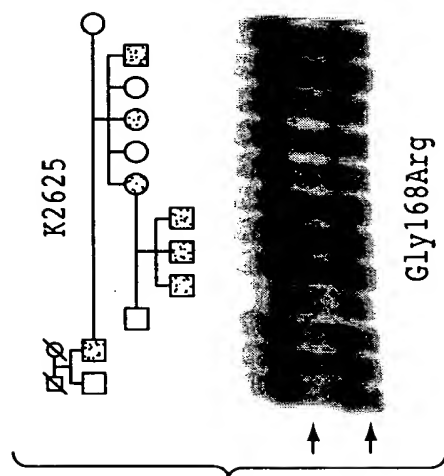


FIG. 12H

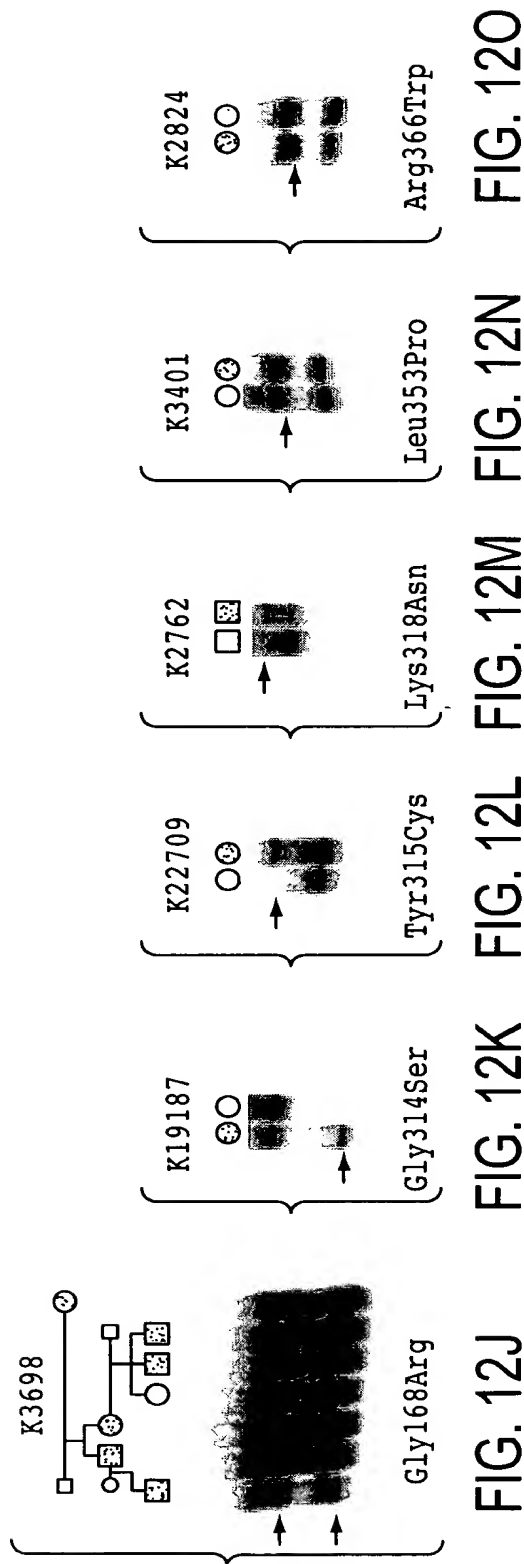


FIG. 12J

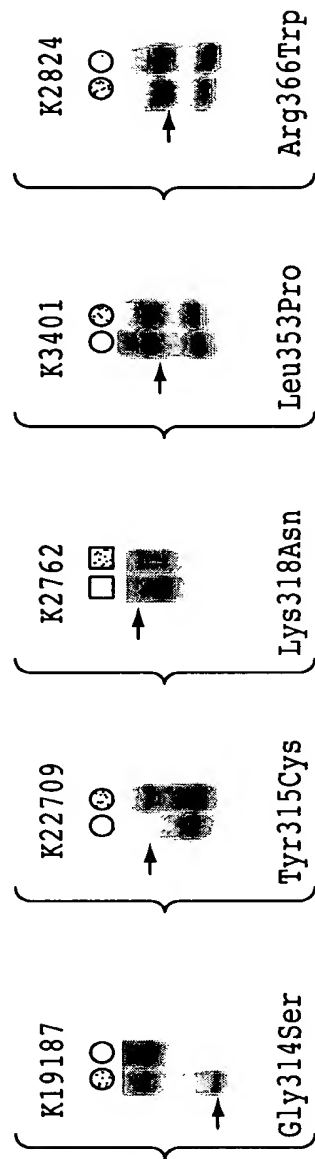


FIG. 12K

FIG. 12L

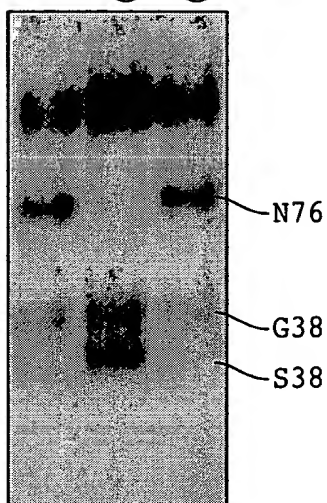
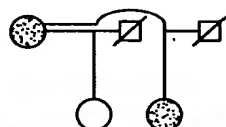
FIG. 12M

FIG. 12N

FIG. 12O



K1789

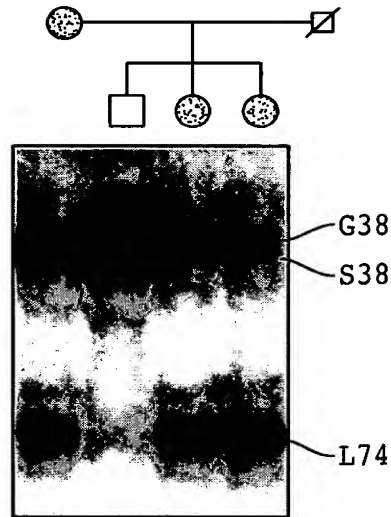


NORMAL	CAC H	TCG S	AAC N	GAC D	CCA P	TTC F	AAC N
MUTANT	CAC H	TCG S	AAC N	AAC N	CCA P	TTC F	AAC N

FIG. 13A



K1754



NORMAL	CTG	GAG	CAC	TCG	AAC	GAC	CCA
	L	E	H	S	N	D	P
				↓			
MUTANT	CTG	GAG	CAC	TTG	AAC	GAC	CCA
	L	E	H	L	N	D	P

FIG. 13B



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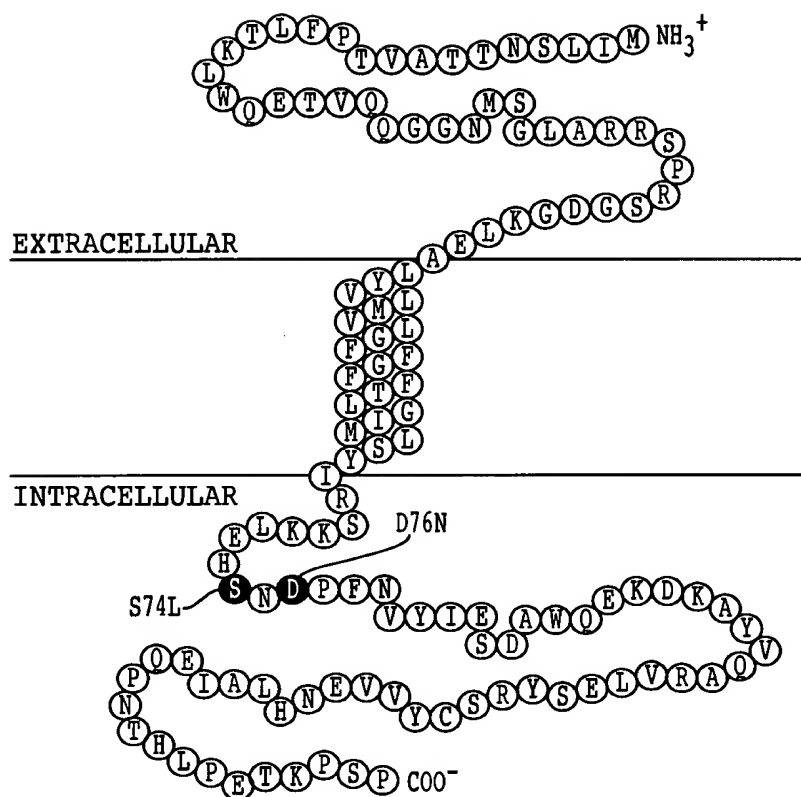


FIG. 13C

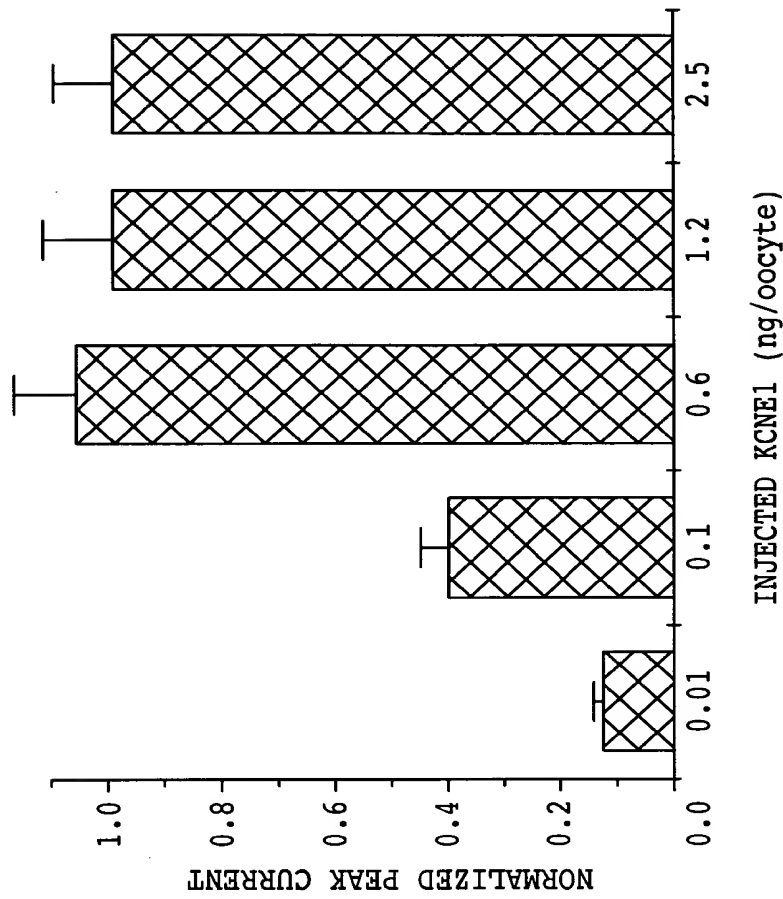


FIG. 14B

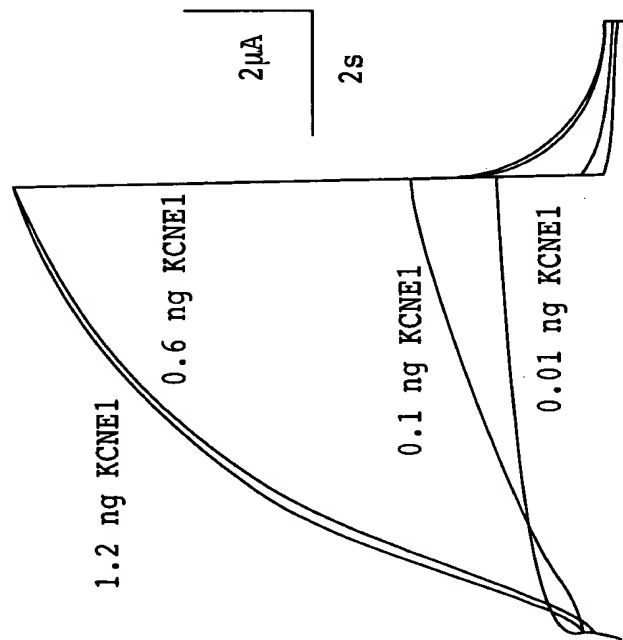


FIG. 14A

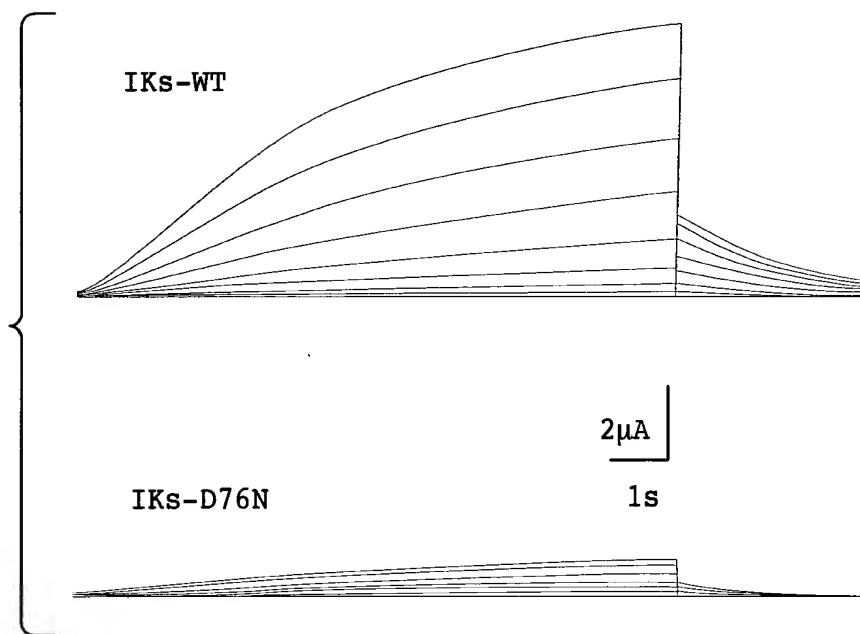


FIG. 15A

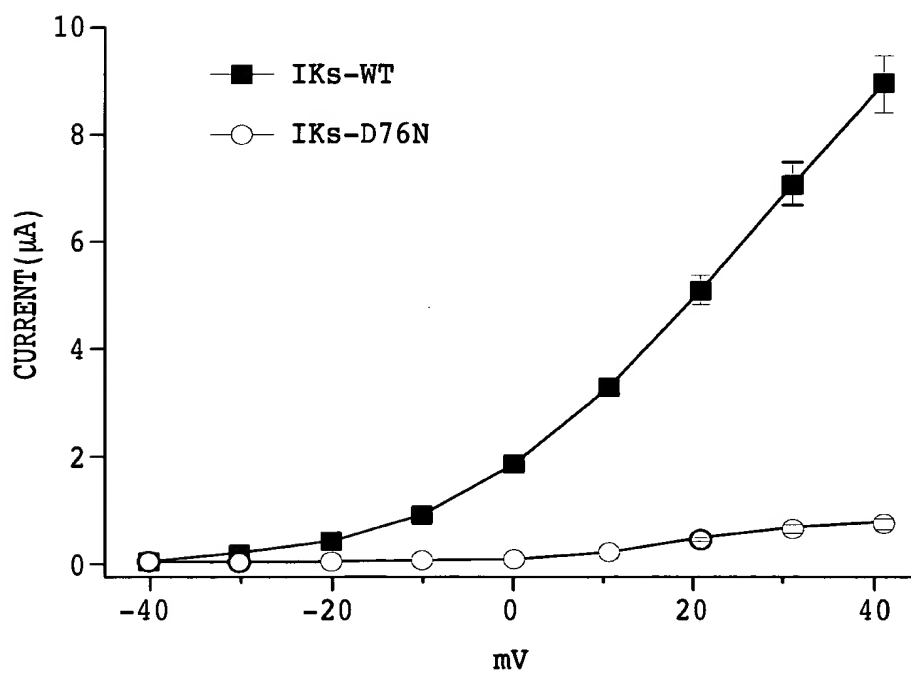


FIG. 15B

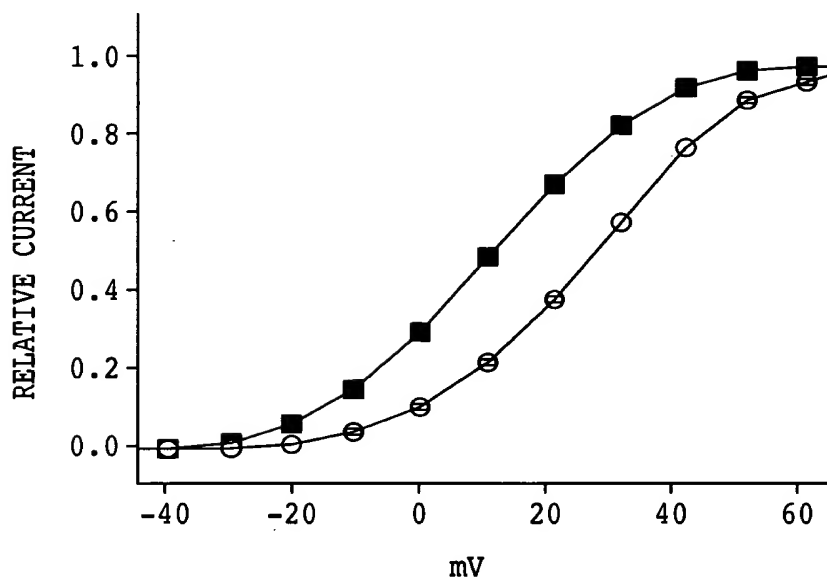


FIG. 15C

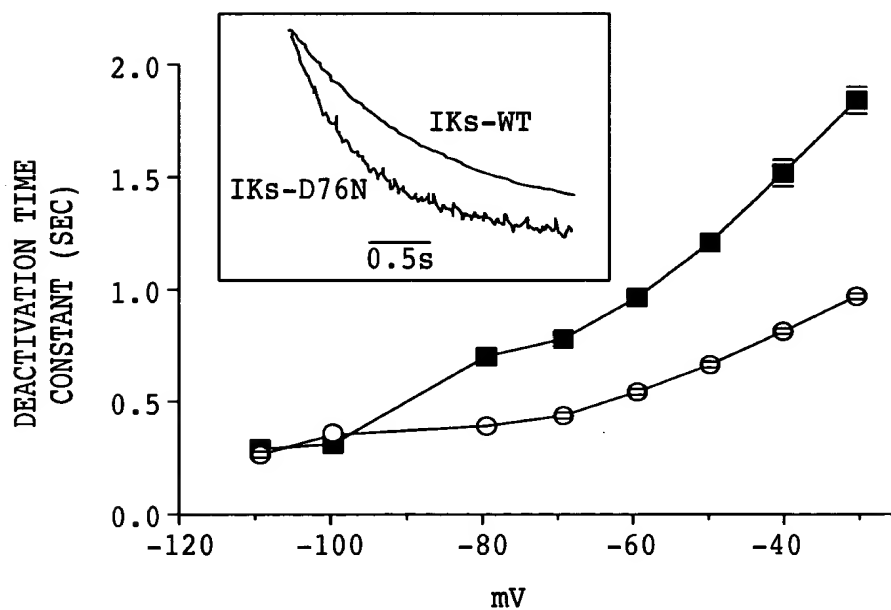


FIG. 15D

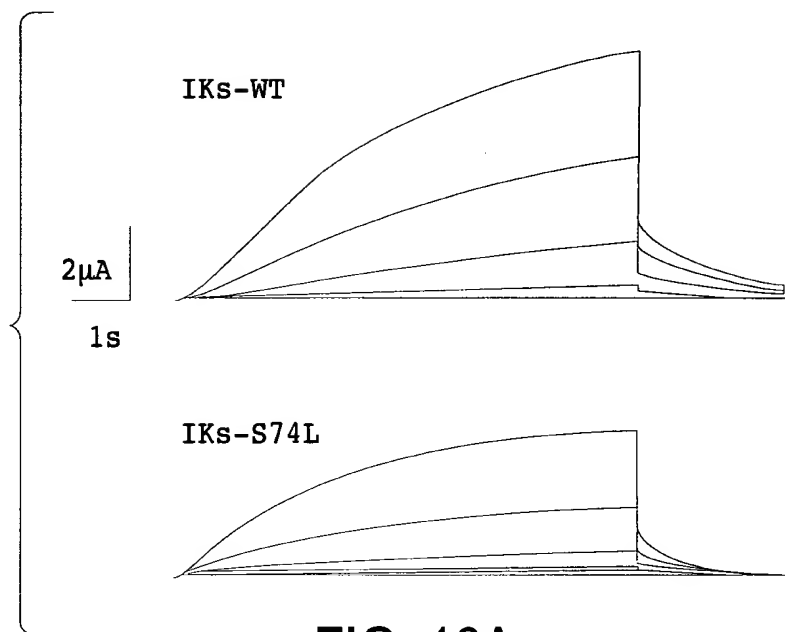


FIG. 16A

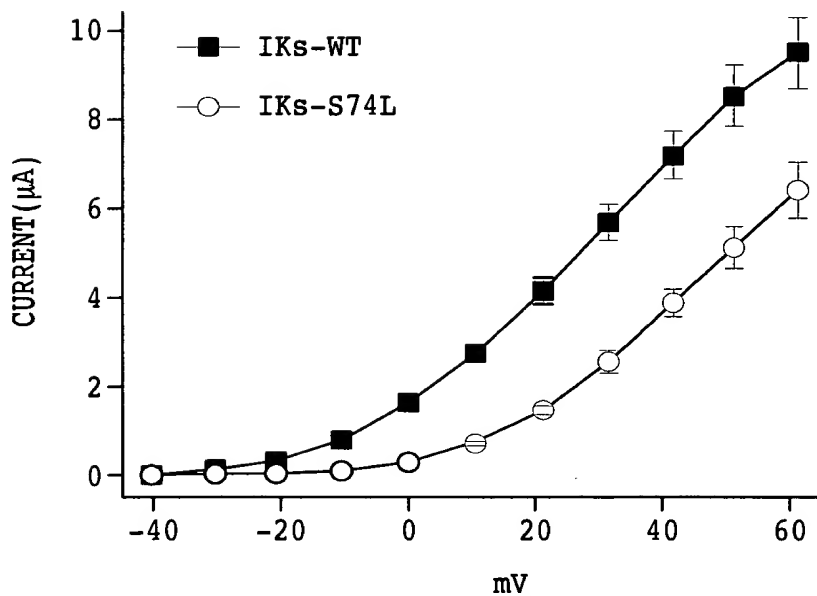


FIG. 16B

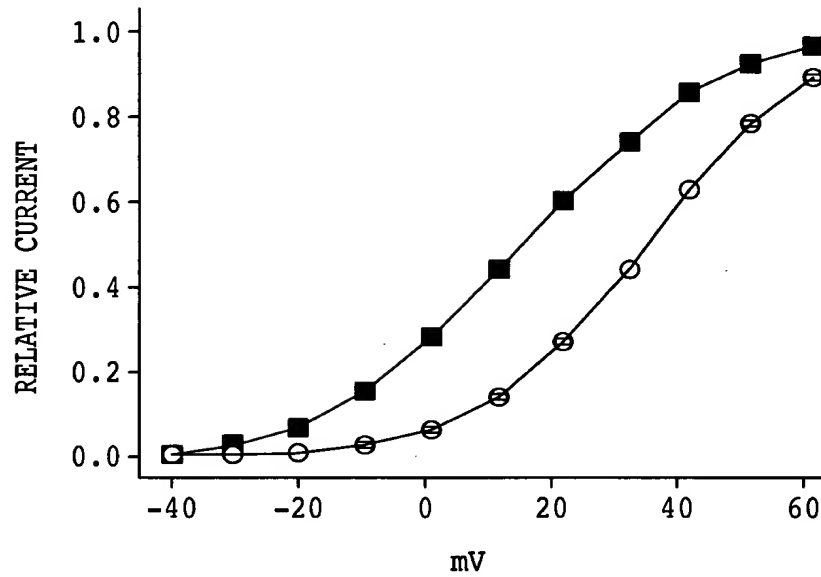


FIG. 16C

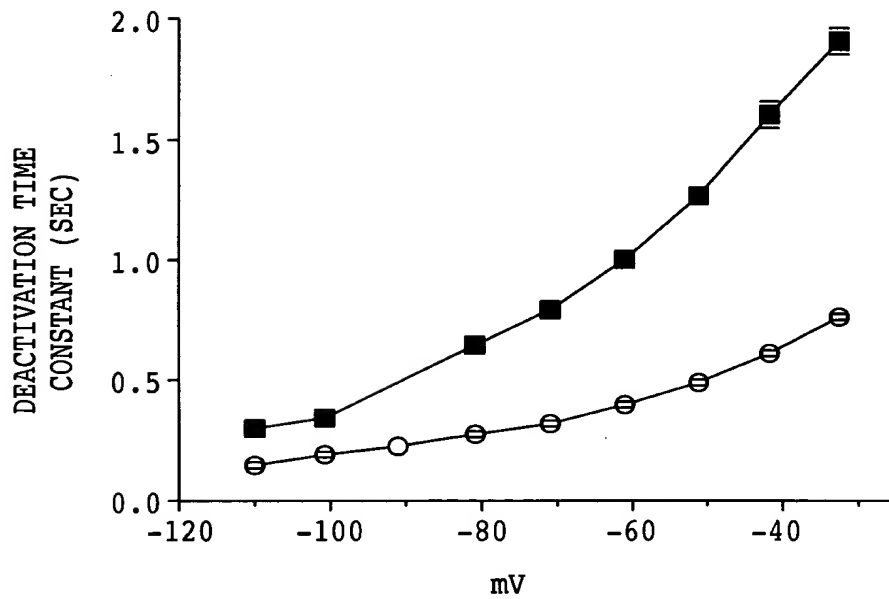


FIG. 16D

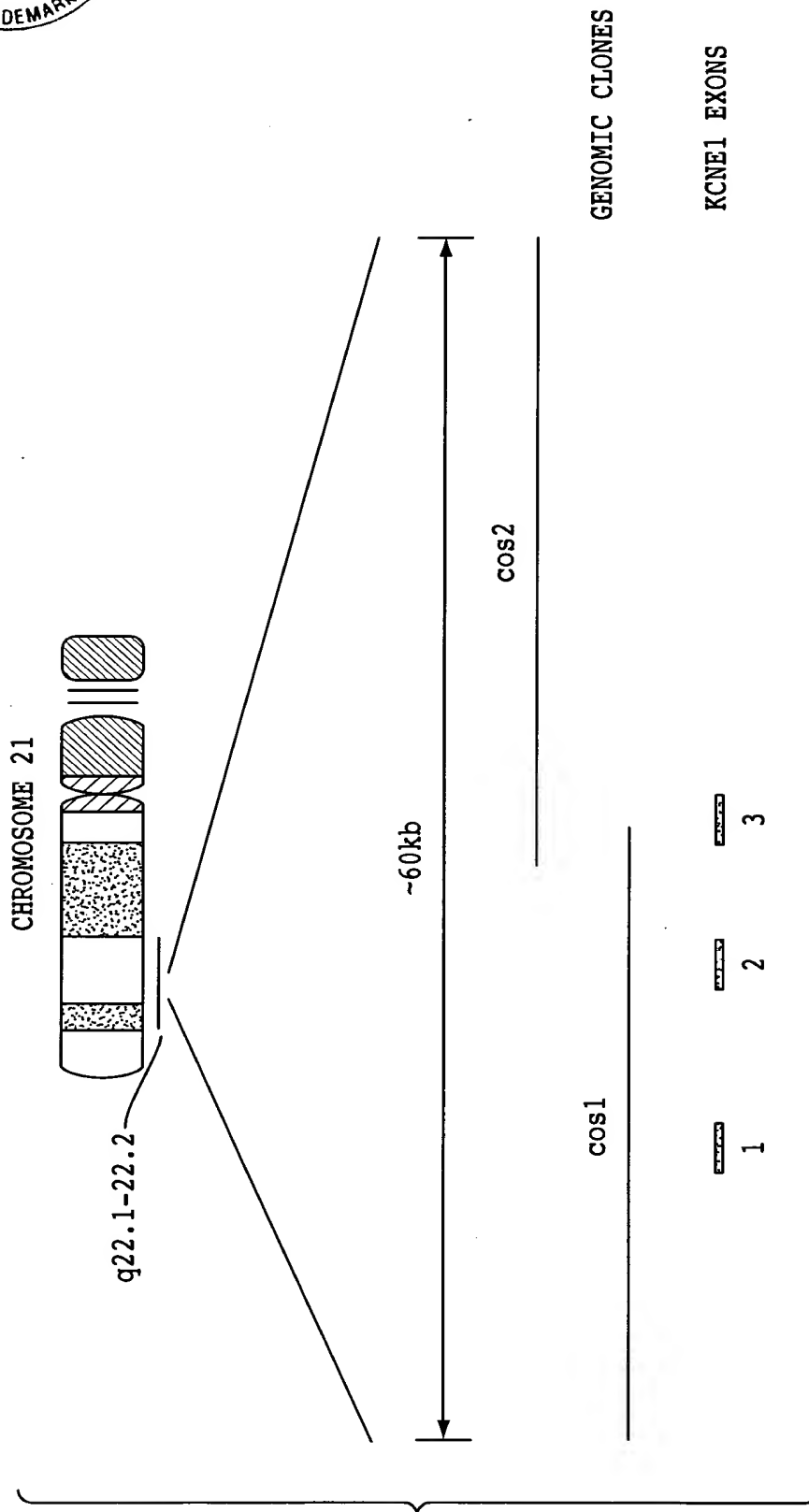


FIG. 17



ACACCCGGCTCTCTCGGCATCTCAGACCCGGGAAAAATCCCTCTGCTTTCTCTGGCCAGTTTCACACAATCATCAGGTGAG-81
CCGAGGATCCATTGGAGGAAGGCATTATCTGTATCCAGAGGAAATAGCCAAGGATATTCAGAGGTGTGCCTGGGAAGTTTG-162
AGCTGCAGCAGTGGAACCTTAATGCCCAGGATGATCCTGTCTAACACCACAGCGGTGACGCCCTTTCTGACCAAGCTGTGG-243
CAGGAGACAGTTCAGCAGGGTGGCAACATGTTCGGGCCTGGCCCCAGGTCCCCCGCAGCGGTGACGGCAAGCTGGAGGCC-324
Q E T V Q Q G G N M S G L A R R S P R S G D G K L E A -44
CTCTACGTCCTCATGGTACTGGGATTCTTCGGCTTCTTCACCTGGGCATCATGCTGAGCTACATCCGCTCCAAGAAGCTG-405
L Y V L M V L G F F G F F T L G I M L S Y I R S K K L -71
GAGCACTCGAACGACCCATTCAACGTCTACATCGAGTCCGATGCCTGGCAAGAGAAGGACAAGGCCTATGTCCAGGCCCGG-486
E H S N D P F N V Y I E S D A W Q E K D K A Y V Q A R -98
GTCTGGAGAGCTACAGGTCGTGCTATGTCTGTTGAAAACCATCTGGCCATAGAACAACCAACACACCTTCTGAGACG-567
V L E S Y R S C Y V V E N H L A I E Q P N T H L P E T -125
AAGCCTTCCCCATGAACCCACCCTGGCTAACTGGACACCTCTGCTGGNNNNAGATTTTCTAATCACATTCTCTCA-648
K P S P *
TACTCTTTATTGTGATGGATAACCACTGGATTTCTTTTTGGCTGTTGTAANGGGTGAGGGGTGGATTAATGACACTGTTTCA-729
CTGTTTCTCTAAAATCACGTTCTTTTGTGATAGACTGTGAGTGGTCCCCCATATCTGTCCCTGCCTTGCTAAATTTAGCA-810
GAATCCCTGAGGACATGGCCTCTGAGAATAGCAGCTGCATTTCCAGACTCCCTTGCACTAGCAAGGTTGTGTGACTAAG-891
CCCTGGCCAGTAGGCATGGAAGTGAAGACTGTAATGTCCAAGTAATCCTTGGAAGAAAAGAACGTGCCCTTAACCTA-972
TGTCTGCTTCCAGTGGCTGGATGTGGAGGAGGTGGAGAGCAGTTATGAGACTGGGAAAGTTCGGGGCACTCAAAGAGCC-1053
ACACACATCTGGGCCTGGGCGACGTGGATCCTCCTTACCACCCACCAGGCCAGATTTACAGGAGAGAGAAATCCACTCCAC-1134
TCTTCTTAAGCCACTGTTATTCTGATCTCTGTTAAGGTGCGAGAATCAATGCCCTTACTGATACACCTACCTTATAGGAC-1215
TGAACCTAAAGGCATGACATTTCCATACTTGTACAAGCACACACTGATTCTGCCCTTGTCACTTCTGTGCTCACTCTTGT-1269
GGCTCTATCTCCTCCTGCCCTTCCGCCTTCCACTCCTCCCTTGACCCATCCTGCACACATCTCCCTGAAAACACACAGG-1377
CACATACTCATATACATAGACACACATACACCTCAATCTAGAAAGAACTTGCTTTGTACAGGGCTGAGATGGAGGAG-1458
AAAAAATGCCCCCTTCAAGTGCATACCAAGGGGAAGGTGCTCGGTCACTGTGGGAGCAGGGAAAGTGGCCCCACTCCC-1539
CGAGAGCCAGGGGAAGGAGTGGCTCTGGGCAGAGAGGGACACATAGCACTGGGGTGGCAGGTCCTTTTGAGGTGATGGGCC-1620
GGTTTGTGAGATGAATTGTATCCCCAAAAGACAGGTACCTTCAATGTGACCTAATTGGGAAATAGAGTCTTTGCAGAT-1701
G(A)n -1702

FIG. 18